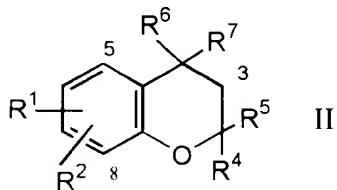


4. A compound of the formula:



wherein

R<sup>1</sup> is OH, O(CH<sub>2</sub>)<sub>1-2</sub>OH, OCH<sub>2</sub>CO<sub>2</sub>H, CO<sub>2</sub>H, O-Z-C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup> or OCH<sub>2</sub>-4-Phe-C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup>;

R<sup>2</sup> is H or lower alkyl;

R<sup>3</sup> is H, alkyl, aryl, or arylalkyl;

R<sup>4</sup> and R<sup>5</sup> are each independently H, lower alkyl, or substituted lower alkyl where the substituents are 1-3 alkoxy, aryl, substituted aryl, carboalkoxy, carboxamido or di-loweralkylamido; or

R<sup>4</sup> and R<sup>5</sup> taken together are -(CH<sub>2</sub>)<sub>n</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-O-(CH<sub>2</sub>)<sub>2</sub>-, -CH<sub>2</sub>-O-(CH<sub>2</sub>)<sub>3</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-NR<sup>8</sup>-CH<sub>2</sub>)<sub>2</sub>-, -CH<sub>2</sub>-NR<sup>8</sup>-(CH<sub>2</sub>)<sub>m</sub>-, -(CH<sub>2</sub>)<sub>2</sub>CH(NHR<sup>8</sup>)(CH<sub>2</sub>)<sub>2</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-S(O)<sub>0-2</sub>-(CH<sub>2</sub>)<sub>2</sub>-, or -CH<sub>2</sub>CH<sub>2</sub>I(N-loweralkyl)(CH<sub>2</sub>)<sub>2</sub>CHCH<sub>2</sub>-,

one of R<sup>6</sup> and R<sup>7</sup> is H and the other is H, OH, or N(CH<sub>2</sub>)<sub>1-6</sub>R<sup>14</sup>R<sup>15</sup>; or

R<sup>6</sup> and R<sup>7</sup> taken together are , with the proviso that

when R<sup>1</sup> is -OH and R<sup>2</sup> is -H, R<sup>6</sup> and R<sup>7</sup> are not -H and -OH or when taken together are

not ,

R<sup>8</sup> is H, COOR<sup>9</sup>, CONHR<sup>10</sup>, CSNHR<sup>11</sup>, COR<sup>12</sup>, SO<sub>2</sub>R<sup>13</sup>, lower alkyl, aryl lower alkyl, heteroaryl, or heteroaryl lower alkyl, wherein aryl is optionally substituted with 1-3 substituents selected from lower alkyl, lower alkoxy, halo, CN, NH<sub>2</sub>, COOH, CONH<sub>2</sub>,

carboalkoxy, and mono- or di-lower alkylamino and wherein heteroaryl is a mono- or bicyclic heteroaromatic ring system of 5 to 10 members including 1 to 3 heteroatoms selected from O, N, and S and 0-3 substituents selected from halo, amino, cyano, lower alkyl, carboalkoxy, CONH<sub>2</sub>, and S-lower alkyl;

R<sup>9</sup> is lower alkyl, aryl, aryl lower alkyl, heteroaryl, aryl substituted by 1-3 substituents selected from alkyl, alkenyl, alkoxy, methylene dioxy, and halo, or a 5- to 6-membered heterocyclic ring containing O or N as a heteroatom, wherein heteroaryl is a heteroaromatic ring of 5 to 6 members including 1 to 2 heteroatoms selected from O, N, and S and 0-2 substituents selected from lower alkyl, dialkylamino, lower alkoxy, and halo;

R<sup>10</sup> and R<sup>11</sup> are each independently lower alkyl, aryl, aryl lower alkyl, or aryl substituted by 1-3 substituents selected from lower alkyl, halo, alkoxy and haloalkyl;

R<sup>12</sup> is lower alkyl, aryl, heteroaryl, aryl lower alkyl, heteroaryl lower alkyl, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N-lower alkyl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, sulfamoyl, lower alkyl sulfamoyl, cyano, and phenyl;

R<sup>13</sup> is lower alkyl, aryl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, CN, and haloalkyl;

R<sup>14</sup> is H, alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl; -CH<sub>2</sub>NR<sup>16</sup>C(O)R<sup>16</sup>; -C(O)NR<sup>16</sup>R<sup>16</sup>; -CH<sub>2</sub>OC(O)R<sup>16</sup>; or -CH<sub>2</sub>SC(O)R<sup>16</sup>;

R<sup>15</sup> is H, alkyl, -C(O)X, -C(S)X, or -C(NCN)NR<sup>3</sup>R<sup>3</sup>;

R<sup>16</sup> is lower alkyl, substituted lower alkyl, aryl, or substituted aryl;

R<sup>17</sup> is H, alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl;

heteroaryl; substituted heteroaryl; heterocycloalkyl;  $-\text{CH}_2\text{NR}^{16}\text{C(O)R}^{16}$ ;  $-\text{C(O)NR}^{16}\text{R}^{16}$ ;  
 $-\text{CH}_2\text{OC(O)R}^{16}$ ; or  $-\text{CH}_2\text{SC(O)R}^{16}$ ;  
X is alkyl, aryl, arylalkyl, O-loweralkyl, or  $-\text{NR}^3\text{R}^3$ ;  
Z is  $-(\text{CH}_2)_{1-6}-$ , optionally substituted with 1-3 lower alkyl;  $-\text{CHR}^2-$ ;  $-\text{Phe-CH}_2-$ , where Phe is  
optionally mono-substituted with halogen, lower alkyl, or alkoxy; or heteroarylene- $(\text{CH}_2)-$ ;  
m is 2 or 3, and  
n is 4-9;  
or a pharmaceutically acceptable salt thereof.

5. A compound of claim 4, wherein R<sup>12</sup> is sulfamoylphenyl.

6. A compound of claim 4, wherein R<sup>12</sup> is p-sulfamoylphenyl.

7. A compound of claim 4, wherein:

R<sup>1</sup> is OH,  $\text{OCH}_2\text{C(O)NH(CH}_2)_1\text{-6R}^{17}$ , or  $\text{OCH}_2\text{-4-Phe-C(O)NH(CH}_2)_1\text{-6R}^{17}$ ;

R<sup>4</sup> and R<sup>5</sup> are each lower alkyl; or

R<sup>4</sup> and R<sup>5</sup> taken together are  $-(\text{CH}_2)_5-$ ,  $-(\text{CH}_2)_2\text{-O-}(\text{CH}_2)_2-$ ,  $-(\text{CH}_2)_2\text{-NR}^8\text{-}(\text{CH}_2)_2-$ ,

$-(\text{CH}_2)_2\text{-CH(NHR}^8\text{)}(\text{CH}_2)_2-$ ,  $-(\text{CH}_2)_2\text{-S-}(\text{CH}_2)_2-$ , or  $\text{CH}_2\text{CH(NCH}_3\text{)}(\text{CH}_2)_2\text{CHCH}_2$  ;

R<sup>6</sup>/R<sup>7</sup> are H/OH or  $-\text{S}(\text{CH}_2)_2\text{S-}$ ;

R<sup>8</sup> is H, COOR<sup>9</sup>, CONHR<sup>10</sup>, CSNHR<sup>11</sup>, COR<sup>12</sup>, SO<sub>2</sub>R<sup>13</sup>, lower alkyl, aryl lower alkyl,  
heteroaryl wherein the heteroatoms include 1 to 3 N atoms and the substituents are halo or  
amino, heteroaryl lower alkyl wherein heteroaryl is 6-membered and the heteroatoms are  
N, or aryl lower alkyl substituted with 1 substituent selected from lower alkyl, alkoxy, and  
halo;

R<sup>9</sup> is lower alkyl, aryl lower alkyl, aryl, tetrahydrofuryl, tetrahydropyranyl, or aryl  
substituted by 1 to 2 substituents selected from lower alkyl, alkenyl, alkoxy, methylene  
dioxy, and halo;

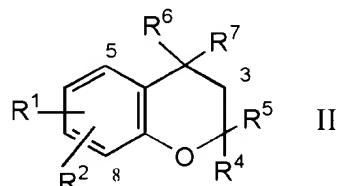
R<sup>10</sup> and R<sup>11</sup> are each independently aryl, aryl lower alkyl, or aryl substituted by 1 substituent selected from lower alkyl, halo, alkoxy, trifluoromethyl, and pentafluoroethyl; R<sup>12</sup> is lower alkyl, aryl, aryl lower alkyl, heteroaryl lower alkyl wherein the heteroatoms are N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from S and N lower alkyl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, halo, sulfamoyl, cyano, or phenyl; and R<sup>13</sup> is lower alkyl, aryl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo; or a pharmaceutically acceptable salt thereof.

38. A compound of claim 4 wherein:

R<sup>1</sup> is OCH<sub>2</sub>CO<sub>2</sub>H;  
R<sup>2</sup> is -H;  
R<sup>4</sup> and R<sup>5</sup> taken together are -(CH<sub>2</sub>)<sub>2</sub>-S-(O)<sub>2</sub>-(CH<sub>2</sub>)<sub>2</sub>-; and  
one of R<sup>6</sup> and R<sup>7</sup> is -H and the other is -H or -N(CH<sub>2</sub>)<sub>1-6</sub>R<sup>14</sup>R<sup>15</sup>.

The foregoing amended claims effect the following changes:

4. (thrice amended) A compound of the formula:



wherein:

R<sup>1</sup> is OH, O(CH<sub>2</sub>)<sub>1-2</sub>OH, OCH<sub>2</sub>CO<sub>2</sub>H, CO<sub>2</sub>H, O-Z-C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup> or OCH<sub>2</sub>-4-Phe-C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup>;

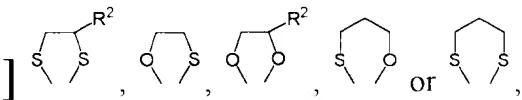
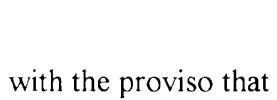
R<sup>2</sup> is H or lower alkyl;

R<sup>3</sup> is H, alkyl, aryl, or arylalkyl;

R<sup>4</sup> and R<sup>5</sup> are each independently H, lower alkyl, or substituted lower alkyl where the substituents are 1-3 alkoxy, aryl, substituted aryl, carboalkoxy, carboxamido or di-loweralkylamido; or

R<sup>4</sup> and R<sup>5</sup> taken together are -(CH<sub>2</sub>)<sub>n</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-O-(CH<sub>2</sub>)<sub>2</sub>-, -CH<sub>2</sub>-O-(CH<sub>2</sub>)<sub>3</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-NR<sup>8</sup>-CH<sub>2</sub>)<sub>2</sub>-, -CH<sub>2</sub>-NR<sup>8</sup>-(CH<sub>2</sub>)<sub>m</sub>-, -(CH<sub>2</sub>)<sub>2</sub>CH(NHR<sup>8</sup>)(CH<sub>2</sub>)<sub>2</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-S(O)<sub>0-2</sub>-(CH<sub>2</sub>)<sub>2</sub>-, or -CH<sub>2</sub>CHI(N<sub>loweralkyl</sub>)(CH<sub>2</sub>)<sub>2</sub>CHCH<sub>2</sub>-,

one of R<sup>6</sup> and R<sup>7</sup> is H and the other is H, OH, or N(CH<sub>2</sub>)<sub>1-6</sub>R<sup>14</sup>R<sup>15</sup>, or

R<sup>6</sup> and R<sup>7</sup> taken together are [O, ]  , or  , with the proviso that

when R<sup>1</sup> is -OH and R<sup>2</sup> is -H, R<sup>6</sup> and R<sup>7</sup> are not -H and -OH or when taken together are

not  ;

R<sup>8</sup> is H, COOR<sup>9</sup>, CONHR<sup>10</sup>, CSNHR<sup>11</sup>, COR<sup>12</sup>, SO<sub>2</sub>R<sup>13</sup>, lower alkyl, aryl lower alkyl, heteroaryl, or heteroaryl lower alkyl, wherein aryl is optionally substituted with 1-3 substituents selected from lower alkyl, lower alkoxy, halo, CN, NH<sub>2</sub>, COOH, CONH<sub>2</sub>, carboalkoxy, and mono- or di-lower alkylamino and wherein heteroaryl is a mono- or bicyclic heteroaromatic ring system of 5 to 10 members including 1 to 3 heteroatoms selected from O, N, and S and 0-3 substituents selected from halo, amino, cyano, lower alkyl, carboalkoxy, CONH<sub>2</sub>, and S-lower alkyl;

R<sup>9</sup> is lower alkyl, aryl, aryl lower alkyl, heteroaryl, aryl substituted by 1-3 substituents selected from alkyl, alkenyl, alkoxy, methylene dioxy, and halo, or a 5- to 6-membered heterocyclic ring [wherein the hetero atom is] **containing O or N as a heteroatom**, wherein

heteroaryl is a heteroaromatic ring of 5 to 6 members including 1 to 2 heteroatoms selected from O, N, and S and 0-2 substituents selected from lower alkyl, dialkylamino, lower alkoxy, and halo;

R<sup>10</sup> and R<sup>11</sup> are each independently lower alkyl, aryl, aryl lower alkyl, or aryl substituted by 1-3 substituents selected from lower alkyl, halo, alkoxy and haloalkyl;

R<sup>12</sup> is lower alkyl, aryl, heteroaryl, aryl lower alkyl, heteroaryl lower alkyl, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N-lower alkyl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, sulfamoyl, lower alkyl sulfamoyl, cyano, and phenyl;

R<sup>13</sup> is lower alkyl, aryl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, CN, and haloalkyl;

R<sup>14</sup> is H; alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl; -CH<sub>2</sub>NR<sup>16</sup>C(O)R<sup>16</sup>; -C(O)NR<sup>16</sup>R<sup>16</sup>; -CH<sub>2</sub>OC(O)R<sup>16</sup>; or -CH<sub>2</sub>SC(O)R<sup>16</sup>;

R<sup>15</sup> is H, alkyl, -C(O)X, -C(S)X, or -C(NCN)NR<sup>3</sup>R<sup>3</sup>;

R<sup>16</sup> is lower alkyl, substituted lower alkyl, aryl, or substituted aryl;

R<sup>17</sup> is H; alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl; -CH<sub>2</sub>NR<sup>16</sup>C(O)R<sup>16</sup>; -C(O)NR<sup>16</sup>R<sup>16</sup>; -CH<sub>2</sub>OC(O)R<sup>16</sup>; or -CH<sub>2</sub>SC(O)R<sup>16</sup>;

X is alkyl, aryl, arylalkyl, O-loweralkyl, or -NR<sup>3</sup>R<sup>3</sup>;

Z is -(CH<sub>2</sub>)<sub>1-6</sub>-, optionally substituted with 1-3 lower alkyl; -CHR<sup>2</sup>-; -Phe-CH<sub>2</sub>-; where Phe is optionally mono-substituted with halogen, lower alkyl, or alkoxy; or heteroarylene-(CH<sub>2</sub>)-;

m is 2 or 3; and

n is 4-9;  
or a pharmaceutically acceptable salt thereof.

5. (once amended) A compound of claim 4    wherein R<sup>12</sup> is sulfamoylphenyl.

6. (once amended) A compound of claim 4    wherein R<sup>12</sup> is *p*-sulfamoylphenyl.

7. (once amended) A compound of claim 4    wherein:

R<sup>1</sup> is OH, OCH<sub>2</sub>C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup>, or OCH<sub>2</sub>-4-Phe-C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup>;

R<sup>4</sup> and R<sup>5</sup> are each lower alkyl; or

R<sup>4</sup> and R<sup>5</sup> taken together are -(CH<sub>2</sub>)<sub>5</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-O-(CH<sub>2</sub>)<sub>2</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-NR<sup>8</sup>-(CH<sub>2</sub>)<sub>2</sub>-,

-(CH<sub>2</sub>)<sub>2</sub>-CH(NHR<sup>8</sup>)(CH<sub>2</sub>)<sub>2</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-S-(CH<sub>2</sub>)<sub>2</sub>-, or -CH<sub>2</sub>CH(NCH<sub>3</sub>)(CH<sub>2</sub>)<sub>2</sub>CHCH<sub>2</sub>- ;

R<sup>6</sup>/R<sup>7</sup> are H/OH [ ; =O , ] or -S(CH<sub>2</sub>)<sub>2</sub>S-;

R<sup>8</sup> is H, COOR<sup>9</sup>, CONHR<sup>10</sup>, CSNHR<sup>11</sup>, COR<sup>12</sup>, SO<sub>2</sub>R<sup>13</sup>, lower alkyl, aryl lower alkyl, heteroaryl wherein the [ ring members ] **heteroatoms** include 1 to 3 N atoms and the substituents are halo or amino, heteroaryl lower alkyl wherein heteroaryl is 6-membered and the heteroatoms are N, or aryl lower alkyl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo;

R<sup>9</sup> is lower alkyl, aryl lower alkyl, aryl, tetrahydrofuranyl, tetrahydropyranyl, or aryl substituted by 1 to 2 substituents selected from lower alkyl, alkenyl, alkoxy, methylene dioxo, and halo;

R<sup>10</sup> and R<sup>11</sup> are each independently aryl, aryl lower alkyl, or aryl substituted by 1 substituent selected from lower alkyl, halo, alkoxy, trifluoromethyl, and pentafluoroethyl;

R<sup>12</sup> is lower alkyl, aryl, aryl lower alkyl, heteroaryl lower alkyl wherein the heteroatoms are N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from S and N

lower alkyl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, halo, sulfamoyl, cyano, or phenyl; **and**

R<sup>13</sup> is lower alkyl, aryl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo;  
or a pharmaceutically acceptable salt thereof.

38. (once amended) A compound of claim 4 wherein:

R<sup>1</sup> is OCH<sub>2</sub>CO<sub>2</sub>H;

R<sup>2</sup> is -H,

R<sup>4</sup> and R<sup>5</sup> taken together are -(CH<sub>2</sub>)<sub>2</sub>-S-(O)<sub>2</sub>-(CH<sub>2</sub>)<sub>2</sub>-; **and**

one of R<sup>6</sup> and R<sup>7</sup> is -H and the other is -H or -N(CH<sub>2</sub>)<sub>1-6</sub>R<sup>14</sup>R<sup>15</sup> [ ;

R<sup>14</sup> is -H, and

R<sup>15</sup> is alkyl ].

### III. New Claims

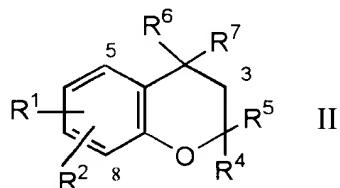
Please add new claims 39-49.

39. A compound of claim 38 wherein:

R<sup>14</sup> is -H, and

R<sup>15</sup> is alkyl.

40. A compound of the formula:



wherein:

R<sup>1</sup> is OCH<sub>2</sub>CO<sub>2</sub>H;

R<sup>2</sup> is H;

R<sup>4</sup> and R<sup>5</sup> taken together are -(CH<sub>2</sub>)<sub>2</sub>-S-(O)<sub>2</sub>-(CH<sub>2</sub>)<sub>2</sub>-, and

one of R<sup>6</sup> and R<sup>7</sup> is -H and the other is -H or -N(CH<sub>2</sub>)<sub>1-6</sub>R<sup>14</sup>R<sup>15</sup>,

wherein:

R<sup>14</sup> is H; alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl; -CH<sub>2</sub>NR<sup>16</sup>C(O)R<sup>16</sup>; -C(O)NR<sup>16</sup>R<sup>16</sup>; -CH<sub>2</sub>OC(O)R<sup>16</sup>; or -CH<sub>2</sub>SC(O)R<sup>16</sup>;

wherein:

R<sup>16</sup> is lower alkyl, substituted lower alkyl, aryl, or substituted aryl; and

R<sup>15</sup> is H, alkyl, -C(O)X, -C(S)X, or -C(NCN)NR<sup>3</sup>R<sup>3</sup>;

wherein:

X is alkyl, aryl, arylalkyl, O-loweralkyl, or -NR<sup>3</sup>R<sup>3</sup>; and

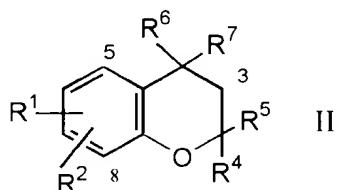
R<sup>3</sup> is H, alkyl, aryl, or arylalkyl.

41. A compound of claim 40, wherein:

R<sup>14</sup> is -H; and

R<sup>15</sup> is alkyl.

42. A compound of the formula:



wherein:

R<sup>1</sup> is OH, O(CH<sub>2</sub>)<sub>1-2</sub>OH, OCH<sub>2</sub>CO<sub>2</sub>H, CO<sub>2</sub>H, O-Z-C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup> or OCH<sub>2</sub>-4-Phe-C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup>;

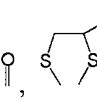
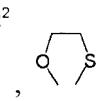
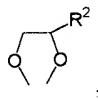
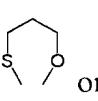
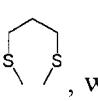
R<sup>2</sup> is H or lower alkyl;

R<sup>3</sup> is H, alkyl, aryl, or arylalkyl;

R<sup>4</sup> and R<sup>5</sup> are each independently H, lower alkyl, or substituted lower alkyl where the substituents are 1-3 alkoxy, aryl, substituted aryl, carboalkoxy, carboxamido or di-loweralkylamido; or

R<sup>4</sup> and R<sup>5</sup> taken together are -(CH<sub>2</sub>)<sub>n</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-O-(CH<sub>2</sub>)<sub>2</sub>-, -CH<sub>2</sub>-O-(CH<sub>2</sub>)<sub>3</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-NR<sup>8</sup>-CH<sub>2</sub>)<sub>2</sub>-, -CH<sub>2</sub>-NR<sup>8</sup>-(CH<sub>2</sub>)<sub>m</sub>-, -(CH<sub>2</sub>)<sub>2</sub>CH(NHR<sup>8</sup>)(CH<sub>2</sub>)<sub>2</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-S(O)<sub>0-2</sub>-(CH<sub>2</sub>)<sub>2</sub>-, or -CH<sub>2</sub>CH(N-loweralkyl)(CH<sub>2</sub>)<sub>2</sub>CHCH<sub>2</sub>-;

one of R<sup>6</sup> and R<sup>7</sup> is H and the other is H, OH, or N(CH<sub>2</sub>)<sub>1-6</sub>R<sup>14</sup>R<sup>15</sup>; or

R<sup>6</sup> and R<sup>7</sup> taken together are , , ,  or , with the proviso that

when R<sup>1</sup> is -OH and R<sup>2</sup> is -H, R<sup>6</sup> and R<sup>7</sup> are not -H and -OH or when taken together are

not  or  and when R<sup>1</sup> is -OCH<sub>2</sub>CO<sub>2</sub>H and R<sup>4</sup> and R<sup>5</sup> are both -H or methyl, R<sup>6</sup> and R<sup>7</sup>

taken together is not 

R<sup>8</sup> is H, COOR<sup>9</sup>, CONHR<sup>10</sup>, CSNHR<sup>11</sup>, COR<sup>12</sup>, SO<sub>2</sub>R<sup>13</sup>, lower alkyl, aryl lower alkyl, heteroaryl, or heteroaryl lower alkyl, wherein aryl is optionally substituted with 1-3 substituents selected from lower alkyl, lower alkoxy, halo, CN, NH<sub>2</sub>, COOH, CONH<sub>2</sub>, carboalkoxy, and mono- or di-lower alkylamino and wherein heteroaryl is a mono- or bicyclic heteroaromatic ring system of 5 to 10 members including 1 to 3 heteroatoms selected from O, N, and S and 0-3 substituents selected from halo, amino, cyano, lower

alkyl, carboalkoxy, CONH<sub>2</sub>, and S-lower alkyl;

R<sup>9</sup> is lower alkyl, aryl, aryl lower alkyl, heteroaryl, aryl substituted by 1-3 substituents selected from alkyl, alkenyl, alkoxy, methylene dioxy, and halo, or a 5- to 6-membered heterocyclic ring containing O or N as a heteroatom, wherein heteroaryl is a heteroaromatic ring of 5 to 6 members including 1 to 2 heteroatoms selected from O, N, and S and 0-2 substituents selected from lower alkyl, dialkylamino, lower alkoxy, and halo;

R<sup>10</sup> and R<sup>11</sup> are each independently lower alkyl, aryl, aryl lower alkyl, or aryl substituted by 1-3 substituents selected from lower alkyl, halo, alkoxy and haloalkyl;

R<sup>12</sup> is lower alkyl, aryl, heteroaryl, aryl lower alkyl, heteroaryl lower alkyl, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N-lower alkyl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, sulfamoyl, lower alkyl sulfamoyl, cyano, and phenyl;

R<sup>13</sup> is lower alkyl, aryl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, CN, and haloalkyl;

R<sup>14</sup> is H; alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl, substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl; -CH<sub>2</sub>NR<sup>16</sup>C(O)R<sup>16</sup>; -C(O)NR<sup>16</sup>R<sup>16</sup>; -CH<sub>2</sub>OC(O)R<sup>16</sup>; or -CH<sub>2</sub>SC(O)R<sup>16</sup>;

R<sup>15</sup> is H, alkyl, -C(O)X, -C(S)X, or -C(NCN)NR<sup>3</sup>R<sup>3</sup>;

R<sup>16</sup> is lower alkyl, substituted lower alkyl, aryl, or substituted aryl;

R<sup>17</sup> is H; alkyl, alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl; -CH<sub>2</sub>NR<sup>16</sup>C(O)R<sup>16</sup>; -C(O)NR<sup>16</sup>R<sup>16</sup>; -CH<sub>2</sub>OC(O)R<sup>16</sup>; or -CH<sub>2</sub>SC(O)R<sup>16</sup>;

X is alkyl, aryl, arylalkyl, O-loweralkyl, or -NR<sup>3</sup>R<sup>3</sup>;

Z is -(CH<sub>2</sub>)<sub>1-6</sub>-, optionally substituted with 1-3 lower alkyl; -CHR<sup>2</sup>-, -Phe-CH<sub>2</sub>-, where Phe is

optionally mono-substituted with halogen, lower alkyl, or alkoxy; or heteroarylene-(CH<sub>2</sub>)-;  
m is 2 or 3; and  
n is 4-9;  
or a pharmaceutically acceptable salt thereof.

43. A compound of claim 42, wherein R<sup>12</sup> is sulfamoylphenyl.

44. A compound of claim 42, wherein R<sup>12</sup> is *p*-sulfamoylphenyl.

45. A compound of claim 42, wherein:

R<sup>1</sup> is OH, OCH<sub>2</sub>C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup>, or OCH<sub>2</sub>-4-Phe-C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup>;

R<sup>4</sup> and R<sup>5</sup> are each lower alkyl; or

R<sup>4</sup> and R<sup>5</sup> taken together are -(CH<sub>2</sub>)<sub>5</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-O-(CH<sub>2</sub>)<sub>2</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-NR<sup>8</sup>-(CH<sub>2</sub>)<sub>2</sub>-,  
-(CH<sub>2</sub>)<sub>2</sub>-CH(NHR<sup>8</sup>)(CH<sub>2</sub>)<sub>2</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-S-(CH<sub>2</sub>)<sub>2</sub>-, or -CH<sub>2</sub>CH(NCH<sub>3</sub>)(CH<sub>2</sub>)<sub>2</sub>CHCH<sub>2</sub>- ;

R<sup>6</sup>/R<sup>7</sup> are H/OH; =O, or -S(CH<sub>2</sub>)<sub>2</sub>S-,

R<sup>8</sup> is H, COOR<sup>9</sup>, CONHR<sup>10</sup>, CSNHR<sup>11</sup>, COR<sup>12</sup>, SO<sub>2</sub>R<sup>13</sup>, lower alkyl, aryl lower alkyl, heteroaryl wherein the heteroatoms include 1 to 3 N atoms and the substituents are halo or amino, heteroaryl lower alkyl wherein heteroaryl is 6-membered and the heteroatoms are N, or aryl lower alkyl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo;

R<sup>9</sup> is lower alkyl, aryl lower alkyl, aryl, tetrahydrofuranyl, tetrahydropyranyl, or aryl substituted by 1 to 2 substituents selected from lower alkyl, alkenyl, alkoxy, methylene dioxo, and halo;

R<sup>10</sup> and R<sup>11</sup> are each independently aryl, aryl lower alkyl, or aryl substituted by 1 substituent selected from lower alkyl, halo, alkoxy, trifluoromethyl, and pentafluoroethyl;

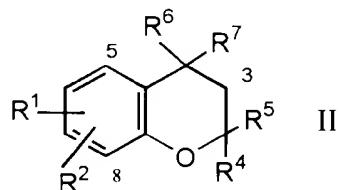
R<sup>12</sup> is lower alkyl, aryl, aryl lower alkyl, heteroaryl lower alkyl wherein the heteroatoms are N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from S and N

lower alkyl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, halo, sulfamoyl, cyano, or phenyl; and

R<sup>13</sup> is lower alkyl, aryl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo;

or a pharmaceutically acceptable salt thereof.

46. A compound of the formula:



wherein:

R<sup>1</sup> is O(CH<sub>2</sub>)<sub>1-2</sub>OH, CO<sub>2</sub>H, O-Z-C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup> or OCH<sub>2</sub>-4-Phe-C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup>;

R<sup>2</sup> is H or lower alkyl;

R<sup>3</sup> is H, alkyl, aryl, or arylalkyl;

R<sup>4</sup> and R<sup>5</sup> are each independently H, lower alkyl, or substituted lower alkyl where the substituents are 1-3 alkoxy, aryl, substituted aryl, carboalkoxy, carboxamido or di-loweralkylamido; or

R<sup>4</sup> and R<sup>5</sup> taken together are -(CH<sub>2</sub>)<sub>n</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-O-(CH<sub>2</sub>)<sub>2</sub>-, -CH<sub>2</sub>-O-(CH<sub>2</sub>)<sub>3</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-NR<sup>8</sup>-CH<sub>2</sub>)<sub>2</sub>-, -CH<sub>2</sub>-NR<sup>8</sup>-(CH<sub>2</sub>)<sub>m</sub>-, -(CH<sub>2</sub>)<sub>2</sub>CH(NHR<sup>8</sup>)(CH<sub>2</sub>)<sub>2</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-S(O)<sub>0-2</sub>-(CH<sub>2</sub>)<sub>2</sub>-, or CH<sub>2</sub>CH(N-loweralkyl)(CH<sub>2</sub>)<sub>2</sub>CHCH<sub>2</sub>;

one of R<sup>6</sup> and R<sup>7</sup> is H and the other is H, OH, or N(CH<sub>2</sub>)<sub>1-6</sub>R<sup>14</sup>R<sup>15</sup>; or

R<sup>6</sup> and R<sup>7</sup> taken together are , with the proviso that

when R<sup>1</sup> is -OH and R<sup>2</sup> is -H, R<sup>6</sup> and R<sup>7</sup> are not -H and -OH or when taken together are

not ;

R<sup>8</sup> is H, COOR<sup>9</sup>, CONHR<sup>10</sup>, CSNHR<sup>11</sup>, COR<sup>12</sup>, SO<sub>2</sub>R<sup>13</sup>, lower alkyl, aryl lower alkyl, heteroaryl, or heteroaryl lower alkyl, wherein aryl is optionally substituted with 1-3 substituents selected from lower alkyl, lower alkoxy, halo, CN, NH<sub>2</sub>, COOH, CONH<sub>2</sub>, carboalkoxy, and mono- or di-lower alkylamino and wherein heteroaryl is a mono- or bicyclic heteroaromatic ring system of 5 to 10 members including 1 to 3 heteroatoms selected from O, N, and S and 0-3 substituents selected from halo, amino, cyano, lower alkyl, carboalkoxy, CONH<sub>2</sub>, and S-lower alkyl;

R<sup>9</sup> is lower alkyl, aryl, aryl lower alkyl, heteroaryl, aryl substituted by 1-3 substituents selected from alkyl, alkenyl, alkoxy, methylene dioxy, and halo, or a 5- to 6-membered heterocyclic ring containing O or N as a heteroatom, wherein heteroaryl is a heteroaromatic ring of 5 to 6 members including 1 to 2 heteroatoms selected from O, N, and S and 0-2 substituents selected from lower alkyl, dialkylamino, lower alkoxy, and halo;

R<sup>10</sup> and R<sup>11</sup> are each independently lower alkyl, aryl, aryl lower alkyl, or aryl substituted by 1-3 substituents selected from lower alkyl, halo, alkoxy and haloalkyl;

R<sup>12</sup> is lower alkyl, aryl, heteroaryl, aryl lower alkyl, heteroaryl lower alkyl, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N-lower alkyl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, sulfamoyl, lower alkyl sulfamoyl, cyano, and phenyl;

R<sup>13</sup> is lower alkyl, aryl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, CN, and haloalkyl;

R<sup>14</sup> is H; alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl; -CH<sub>2</sub>NR<sup>16</sup>C(O)R<sup>16</sup>; -C(O)NR<sup>16</sup>R<sup>16</sup>; -CH<sub>2</sub>OC(O)R<sup>16</sup>; or -CH<sub>2</sub>SC(O)R<sup>16</sup>;

R<sup>15</sup> is H, alkyl, -C(O)X, -C(S)X, or -C(NCN)NR<sup>3</sup>R<sup>3</sup>;  
R<sup>16</sup> is lower alkyl, substituted lower alkyl, aryl, or substituted aryl;  
R<sup>17</sup> is H; alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl; -CH<sub>2</sub>NR<sup>16</sup>C(O)R<sup>16</sup>; -C(O)NR<sup>16</sup>R<sup>16</sup>; -CH<sub>2</sub>OC(O)R<sup>16</sup>; or -CH<sub>2</sub>SC(O)R<sup>16</sup>;  
X is alkyl, aryl, arylalkyl, O-loweralkyl, or -NR<sup>3</sup>R<sup>3</sup>;  
Z is -(CH<sub>2</sub>)<sub>1-6</sub>-, optionally substituted with 1-3 lower alkyl; -CHR<sup>2</sup>-; -Phe-CH<sub>2</sub>-; where Phe is optionally mono-substituted with halogen, lower alkyl, or alkoxy; or heteroarylene-(CH<sub>2</sub>)-;  
m is 2 or 3; and  
n is 4-9;  
or a pharmaceutically acceptable salt thereof.

47. A compound of claim 46, wherein R<sup>12</sup> is sulfamoylphenyl.

48. A compound of claim 46, wherein R<sup>12</sup> is *p*-sulfamoylphenyl.

49. A compound of claim 46, wherein:

R<sup>1</sup> is OCH<sub>2</sub>C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup>, or OCH<sub>2</sub>-4-Phe-C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup>;  
R<sup>4</sup> and R<sup>5</sup> are each lower alkyl; or  
R<sup>4</sup> and R<sup>5</sup> taken together are -(CH<sub>2</sub>)<sub>5</sub>-; -(CH<sub>2</sub>)<sub>2</sub>-O-(CH<sub>2</sub>)<sub>2</sub>-; -(CH<sub>2</sub>)<sub>2</sub>-NR<sup>8</sup>-(CH<sub>2</sub>)<sub>2</sub>-; -(CH<sub>2</sub>)<sub>2</sub>-CH(NHR<sup>8</sup>)(CH<sub>2</sub>)<sub>2</sub>-; -(CH<sub>2</sub>)<sub>2</sub>-S-(CH<sub>2</sub>)<sub>2</sub>-; or CH<sub>2</sub>CH(NCH<sub>3</sub>)(CH<sub>2</sub>)<sub>2</sub>CHCH<sub>2</sub> ;  
R<sup>6</sup>/R<sup>7</sup> are H/OH; =O, or -S(CH<sub>2</sub>)<sub>2</sub>S-;  
R<sup>8</sup> is H, COOR<sup>9</sup>, CONHR<sup>10</sup>, CSNHR<sup>11</sup>, COR<sup>12</sup>, SO<sub>2</sub>R<sup>13</sup>, lower alkyl, aryl lower alkyl, heteroaryl wherein the heteroatoms include 1 to 3 N atoms and the substituents are halo or amino, heteroaryl lower alkyl wherein heteroaryl is 6-membered and the heteroatoms are

N, or aryl lower alkyl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo;

R<sup>9</sup> is lower alkyl, aryl lower alkyl, aryl, tetrahydrofuryl, tetrahydropyranyl, or aryl substituted by 1 to 2 substituents selected from lower alkyl, alkenyl, alkoxy, methylene dioxo, and halo;

R<sup>10</sup> and R<sup>11</sup> are each independently aryl, aryl lower alkyl, or aryl substituted by 1 substituent selected from lower alkyl, halo, alkoxy, trifluoromethyl, and pentafluoroethyl;

R<sup>12</sup> is lower alkyl, aryl, aryl lower alkyl, heteroaryl lower alkyl wherein the heteroatoms are N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from S and N lower alkyl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, halo, sulfamoyl, cyano, or phenyl; and

R<sup>13</sup> is lower alkyl, aryl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo;

or a pharmaceutically acceptable salt thereof.

Remarks

Status of Claims

1-37	Claims of priority application
1-3 and 15-37	Canceled by preliminary amendment
38	Added by July 24, 2000 amendment
8-14	Canceled without prejudice in this paper
39-49	Added in this paper
4-7 and 39-49	Pending following entry of this paper